STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 156375

TO: Rei-Tsang Shiao **Location: 5a10 / 5c18** **Tuesday, June 28, 2005** **Art Unit: 1626** **Phone: 571-272-0707** **Serial Number: 09 / 653563**	**From: Jan Delaval** **Location: Biotech-Chem Library** **Remsen 1a51** **Phone: 571-272-2504** **jan.delaval@uspto.gov**

Search Notes

Jan Delaval for scrh

Access DB# 150215

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Robert (Bob) Shaw Examiner #: 7952 Date: 6/15/05

Art Unit: 1626 Phone Number 30 2-0907 Serial Number: ~~707~~ 09/653,56

Mail Box and Bldg/Room Location: 5A10/3C18 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

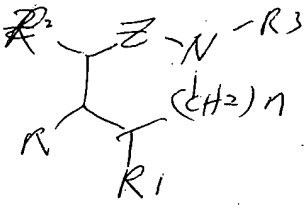
Title of Invention: _____

Inventors (please provide full names): Mann et al

Earliest Priority Filing Date: _____

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

I scrh method of use of comp I



* R1, R2, R3, R are sub

* Z is C

- n is 0

I scrh method of use of comps in claims 170-171, 175~176, and 190-191

****

STAFF USE ONLY

Searcher: _____

Searcher Phone #: 22504

Searcher Location: _____

Date Searcher Picked Up: 6/28/05

Date Completed: 6/28/05

Searcher Prep & Review Time: _____

Clerical Prep Time: 20

Online Time: ~~35~~

Type of Search

NA Sequence (#) _____

AA Sequence (#) _____

Structure (#) ✓

Bibliographic _____

Litigation _____

Fulltext _____

Patent Family _____

Other _____

Vendors and cost where applicable

STN ✓

Dialog _____

Questel/Orbit _____

Dr.Link _____

Lexis/Nexis _____

Sequence Systems _____

WWW/Internet _____

Other (specify) _____

PTO-1590 (8-01)

```
=> fil reg
FILE 'REGISTRY' ENTERED AT 15:44:05 ON 28 JUN 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   27 JUN 2005  HIGHEST RN 853049-67-9
DICTIONARY FILE UPDATES:  27 JUN 2005  HIGHEST RN 853049-67-9

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005.  A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*                                                                    *
**********************************************************************

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> d sta que l61
L5              STR
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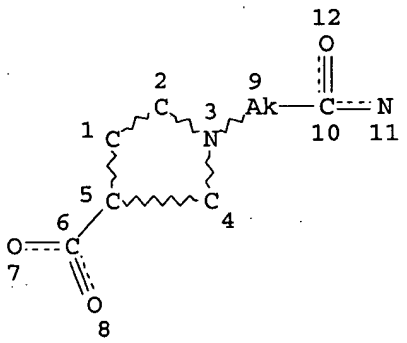


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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC   3
NUMBER OF NODES IS  12

STEREO ATTRIBUTES: NONE
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L7          2808 SEA FILE=REGISTRY SSS FUL L5
L60               STR
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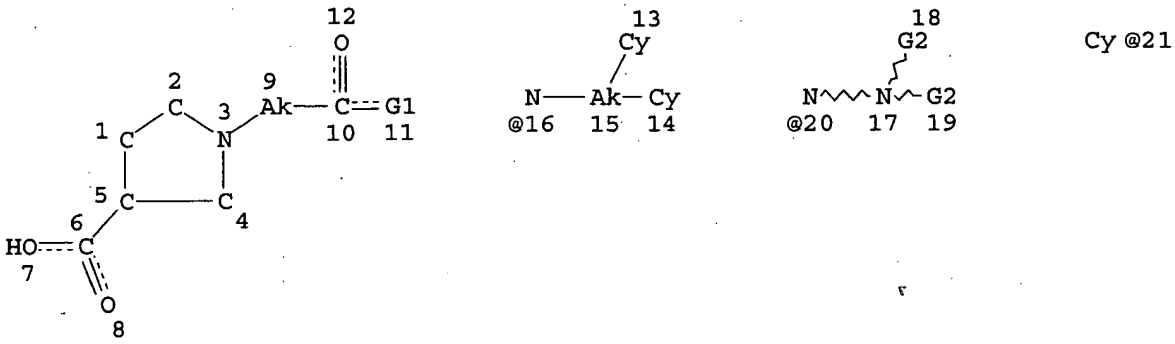


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VAR G2=AK/21
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CONNECT IS M1  RC AT   4
CONNECT IS M1  RC AT  13
CONNECT IS M1  RC AT  14
CONNECT IS M1  RC AT  21
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC   3
NUMBER OF NODES IS  21

STEREO ATTRIBUTES: NONE
L61           22 SEA FILE=REGISTRY SUB=L7 CSS FUL L60

100.0% PROCESSED   2659 ITERATIONS                    22 ANSWERS
SEARCH TIME: 00.00.01


=> d his

     (FILE 'HOME' ENTERED AT 15:11:53 ON 28 JUN 2005)
               SET COST OFF

     FILE 'REGISTRY' ENTERED AT 15:12:09 ON 28 JUN 2005
L1                STR
L2              0 S L1 CSS
L3                STR L1
L4              1 S L3
L5                STR L3
L6             38 S L5
L7           2808 S L5 FUL
                  SAV L7 SHIAO653/A

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L8              6 S (US94-293349# OR US94-334717# OR US95-442575# OR US95-497998#
L9              1 S US2000-653563#/AP,PRN
                  E WINN M/AU
L10           155 S E3-E9,E13
                  E BOYD S/AU
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L11          101 S E3,E4
                 E BOYD STEVE/AU
L12           60 S E4,E5
                 E HUTCHINS C/AU
L13           70 S E3,E10,E13,E16,E17
                 E JAE H/AU
L14           43 S E5,E13,E14
                 E TASKER A/AU
L15           63 S E3,E8,E9
                 E ON GELDERN T/AU
                 E VON GELDERN T/AU
L16           92 S E3-E8
                 E VONGELDERN T/AU
L17            3 S E4
                 E GELDERN T/AU
L18            1 S E4
                 E KESTER J/AU
L19           25 S E3,E11-E14
                 E SORENSEN B/AU
L20           16 S E3,E8
L21           40 S E46
                 E SZCZEPANKIEWICZ B/AU
L22           43 S E4-E7
                 E HENRY K/AU
                 E SZCZEPANKIEWICZ B/AU
L23            1 S E2
                 E HENRY K/AU
L24           15 S E3,E7
L25           34 S E35,E37-E39
                 E LIU G/AU
L26          843 S E3-E29
                 E LIU GANG/AU
L27          869 S LIU GANG?/AU
                 E WITTENBERGER S/AU
L28           61 S E4-E8
                 E KING S/AU
L29           54 S E3,E4
                 E KING STEVE/AU
L30           71 S E3,E4,E7-E9
                 E JANUS T/AU
L31           15 S E4,E6,E7
                 E PADLEY R/AU
L32           28 S E4-E6
                 E ABBOT/PA,CS
L33          147 S E3,E4
                 E ABBOTT/PA,CS
L34         8778 S E3,E4
L35          197 S L7
L36            1 S L9 AND L35
L37           54 S L8-L34 AND L35
L38           54 S L36,L37
L39            0 S L38 AND (PY<=1994 AND PRY<=1994 OR AY<=1994)
L40            6 S L35 AND (PY<=1994 AND PRY<=1994 OR AY<=1994)
L41           10 S L35 AND (PY<=1995 AND PRY<=1995 OR AY<=1995)
L42            3 S L38 AND L41
L43            7 S L41 NOT L42
L44            2 S L43 NOT 74/SC,SX
L45            4 S L36,L42

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L46          SEL L45 1- RN :    2839 TERMS
                SET SMARTSELECT OFF

     FILE 'REGISTRY' ENTERED AT 15:35:15 ON 28 JUN 2005
L47         2839 S L46
L48         2273 S L7 AND L47

     FILE 'HCAPLUS' ENTERED AT 15:36:19 ON 28 JUN 2005
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L49          SEL L36 1- RN :     669 TERMS
                SET SMARTSELECT OFF

     FILE 'REGISTRY' ENTERED AT 15:36:20 ON 28 JUN 2005
L50          669 S L49
L51          287 S L7 AND L50
L52            0 S L1 CSS SAM SUB=L7
L53            7 S L1 CSS FUL SUB=L7
                 SAV L53 SHIAO653A/A

     FILE 'HCAOLD' ENTERED AT 15:38:25 ON 28 JUN 2005
L54            0 S L53

     FILE 'HCAPLUS' ENTERED AT 15:38:30 ON 28 JUN 2005
L55            3 S L53
                 S L55 AND L1-L34

     FILE 'REGISTRY' ENTERED AT 15:38:43 ON 28 JUN 2005

     FILE 'HCAPLUS' ENTERED AT 15:38:44 ON 28 JUN 2005
L56            2 S L55 AND L8-L34
                 E HWAN SOO/AU
L57            1 S E5
                 E HWAN S/AU
L58            2 S L56,L57

     FILE 'USPATFULL, USPAT2' ENTERED AT 15:39:58 ON 28 JUN 2005
L59            0 S L53

     FILE 'REGISTRY' ENTERED AT 15:40:17 ON 28 JUN 2005
L60                STR L1
L61           22 S L60 CSS FUL SUB=L7
                   SAV L61 SHIAO653B/A

     FILE 'HCAOLD' ENTERED AT 15:43:06 ON 28 JUN 2005
L62            0 S L61

     FILE 'HCAPLUS' ENTERED AT 15:43:08 ON 28 JUN 2005
L63            3 S L61
L64            2 S L63 AND L8-L34,L56-L58
L65            1 S L63 NOT L64

     FILE 'USPATFULL, USPAT2' ENTERED AT 15:43:54 ON 28 JUN 2005
L66            0 S L61

     FILE 'REGISTRY' ENTERED AT 15:44:05 ON 28 JUN 2005

=> d ide can tot l61
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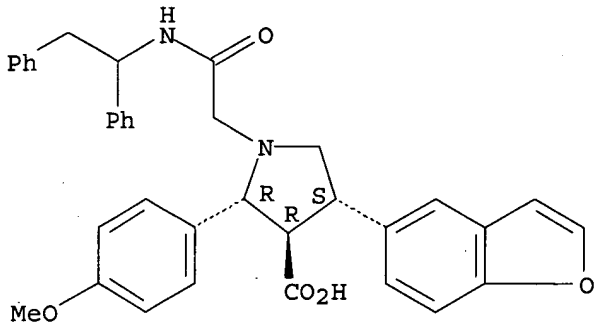
L61 ANSWER 1 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN
RN 697767-60-5 REGISTRY
ED Entered STN: 23 Jun 2004
CN 3-Pyrrolidinecarboxylic acid, 4-(5-benzofuranyl)-1-[2-[(1,2-diphenylethyl)amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C36 H34 N2 O5
SR CA
LC STN Files: CA, CAPLUS

Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

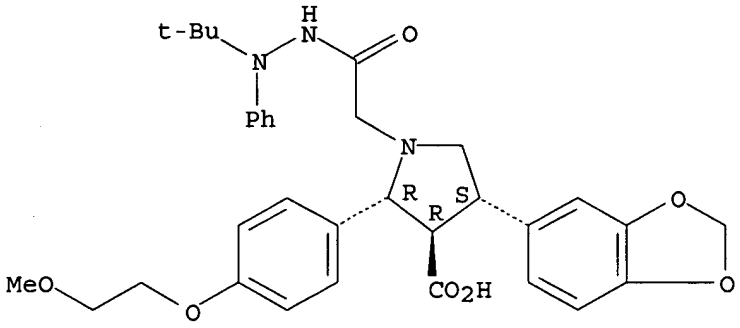
REFERENCE 1: 141:16897

L61 ANSWER 2 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN
RN 403614-32-4 REGISTRY
ED Entered STN: 31 Mar 2002
CN 1-Pyrrolidineacetic acid, 4-(1,3-benzodioxol-5-yl)-3-carboxy-2-[4-(2-methoxyethoxy)phenyl]-, α-[2-(1,1-dimethylethyl)-2-phenylhydrazide], (2R,3R,4S)-rel-, monoacetate (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C33 H39 N3 O7 . C2 H4 O2
SR CA
LC STN Files: CA, CAPLUS

CM 1

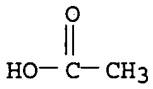
CRN 403614-31-3
CMF C33 H39 N3 O7

Relative stereochemistry.



CM 2

CRN 64-19-7
CMF C2 H4 O2

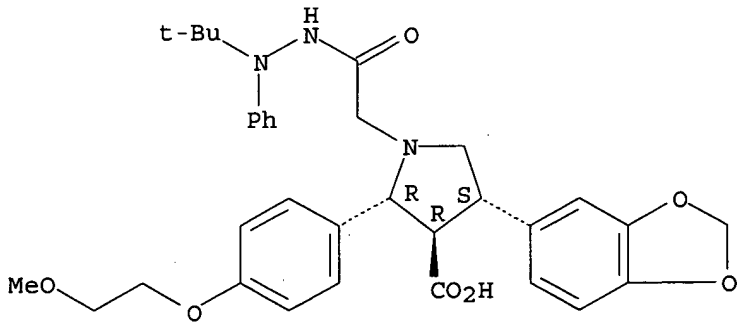


1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:232311

L61 ANSWER 3 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN
RN 403614-31-3 REGISTRY
ED Entered STN: 31 Mar 2002
CN 1-Pyrrolidineacetic acid, 4-(1,3-benzodioxol-5-yl)-3-carboxy-2-[4-(2-methoxyethoxy)phenyl]-, α-[2-(1,1-dimethylethyl)-2-phenylhydrazide], (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C33 H39 N3 O7
CI COM
SR CA
LC STN Files: CA, CAPLUS

Relative stereochemistry.



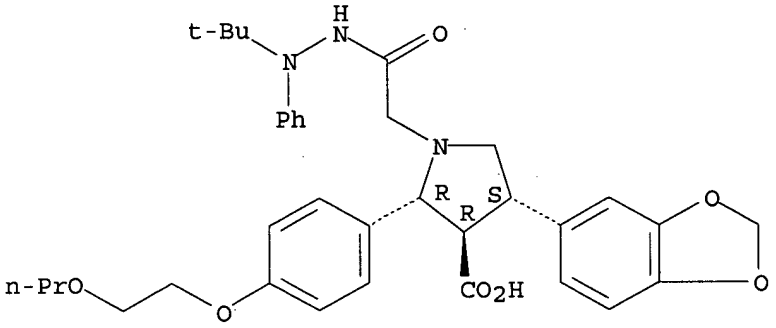
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:232311

L61 ANSWER 4 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN
RN 403614-30-2 REGISTRY
ED Entered STN: 31 Mar 2002
CN 1-Pyrrolidineacetic acid, 4-(1,3-benzodioxol-5-yl)-3-carboxy-2-[4-(2-propoxyethoxy)phenyl]-, α-[2-(1,1-dimethylethyl)-2-phenylhydrazide], (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C35 H43 N3 O7
SR CA
LC STN Files: CA, CAPLUS

Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

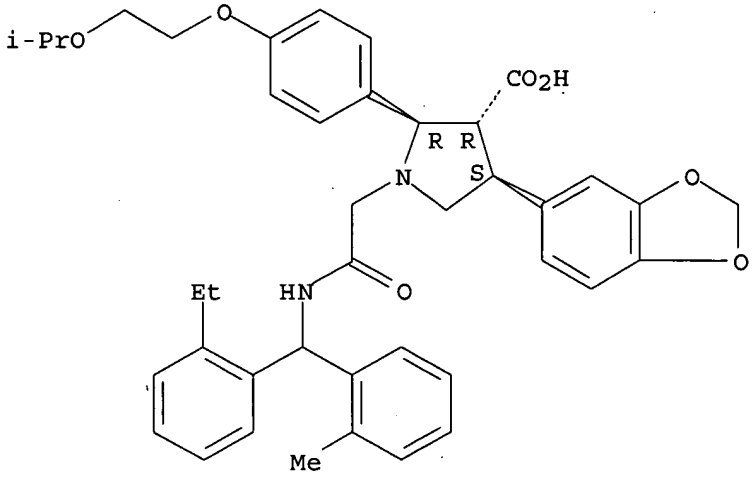
REFERENCE 1: 136:232311

L61 ANSWER 5 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN
RN 403614-29-9 REGISTRY
ED Entered STN: 31 Mar 2002
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[(2-ethylphenyl)(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-[4-[2-(1-methylethoxy)ethoxy]phenyl]-, (2R,3R,4S)-rel-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C41 H46 N2 O7 . C2 H F3 O2
SR CA
LC STN Files: CA, CAPLUS

CM 1

CRN 246853-83-8
CMF C41 H46 N2 O7

Relative stereochemistry.



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CRN 76-05-1
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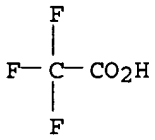


1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

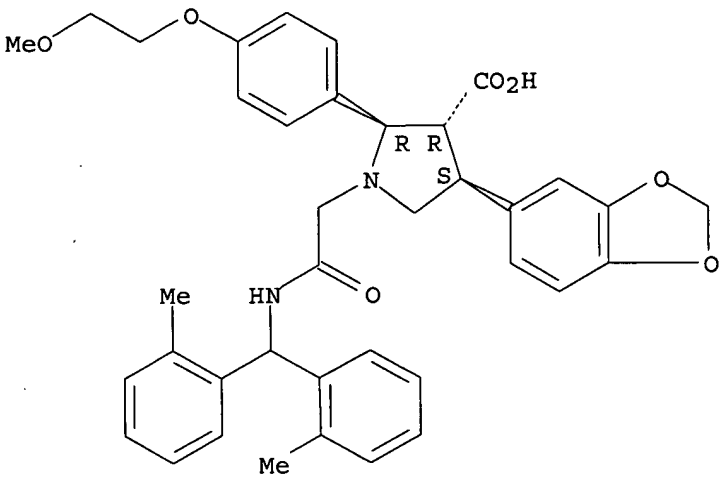
REFERENCE 1: 136:232311

L61 ANSWER 6 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN
RN 403614-26-6 REGISTRY
ED Entered STN: 31 Mar 2002
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-[4-(2-methoxyethoxy)phenyl]-, (2R,3R,4S)-rel-, trifluoroacetate (5:1) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C38 H40 N2 O7 . 1/5 C2 H F3 O2
SR CA
LC STN Files: CA, CAPLUS

CM 1

CRN 246853-81-6
CMF C38 H40 N2 O7

Relative stereochemistry.



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CRN 76-05-1
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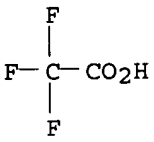


1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

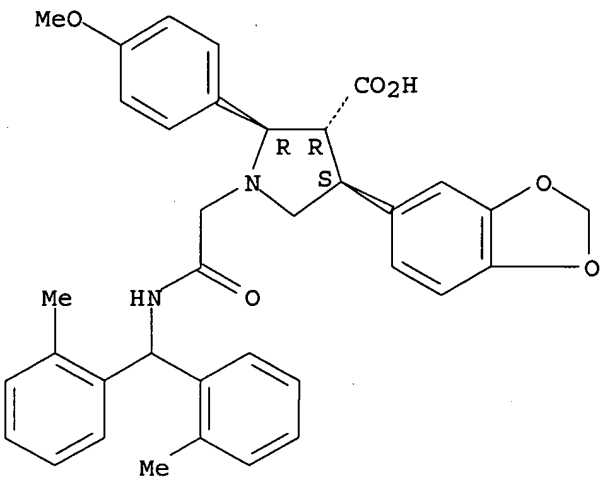
REFERENCE 1: 136:232311

L61 ANSWER 7 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN
RN 403614-24-4 REGISTRY
ED Entered STN: 31 Mar 2002
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel-, trifluoroacetate (5:2) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C36 H36 N2 O6 . 2/5 C2 H F3 O2
SR CA
LC STN Files: CA, CAPLUS

CM 1

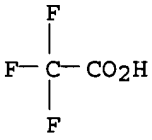
CRN 246853-46-3
CMF C36 H36 N2 O6

Relative stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

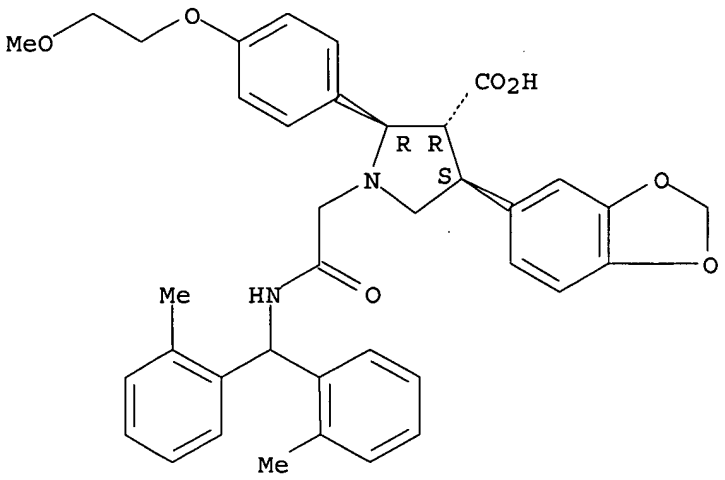


1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:232311

L61 ANSWER 8 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN
RN 246853-85-0 REGISTRY
ED Entered STN: 09 Nov 1999
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-[4-(2-methoxyethoxy)phenyl]-, (2R,3R,4S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C38 H40 N2 O7
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry. Rotation (+).



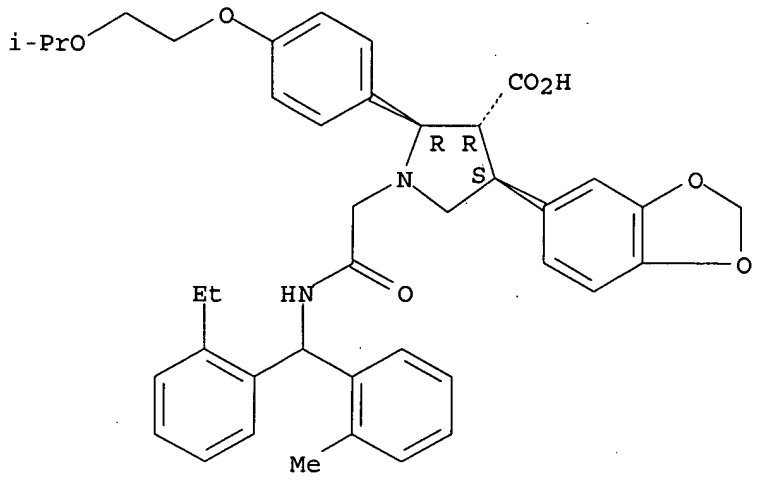
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:286357

L61 ANSWER 9 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN
RN 246853-83-8 REGISTRY
ED Entered STN: 09 Nov 1999
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[(2-ethylphenyl)(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-[4-[2-(1-methylethoxy)ethoxy]phenyl]-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C41 H46 N2 O7
CI COM
SR CA
LC STN Files: CA, CAPLUS

Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:232311

REFERENCE 2: 131:286357

L61 ANSWER 10 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN
RN 246853-82-7 REGISTRY
ED Entered STN: 09 Nov 1999
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-[4-[2-(1-methylethoxy)ethoxy]phenyl]-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)
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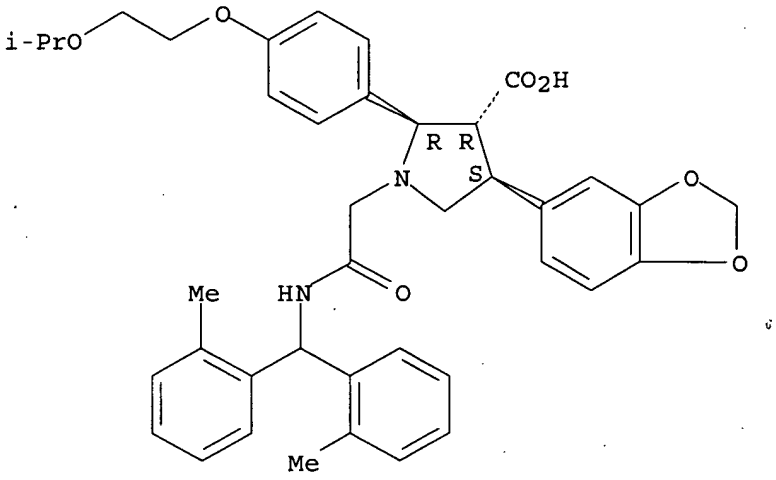
MF C40 H44 N2 O7
SR CA
LC STN Files: CA, CAPLUS

Relative stereochemistry.



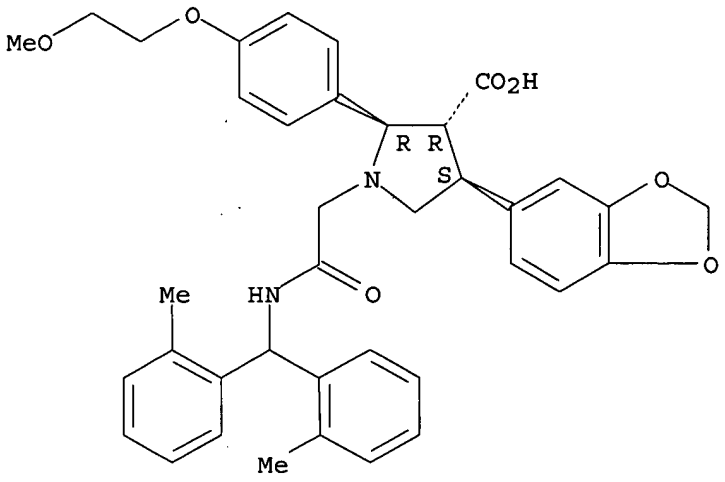
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:286357

L61 ANSWER 11 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN
RN 246853-81-6 REGISTRY
ED Entered STN: 09 Nov 1999
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-[4-(2-methoxyethoxy)phenyl]-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C38 H40 N2 O7
CI COM
SR CA
LC STN Files: CA, CAPLUS

Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:232311

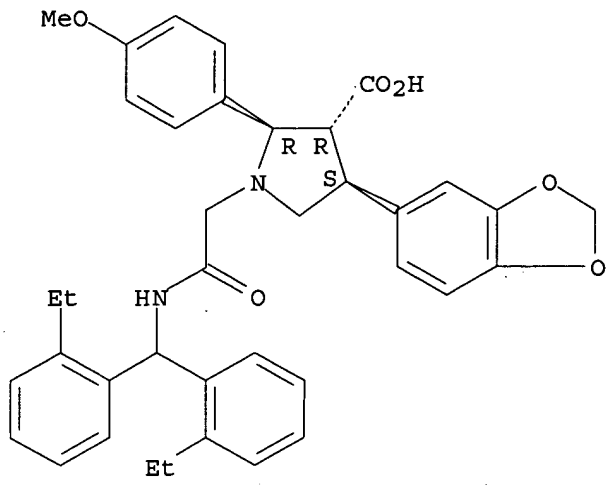
REFERENCE 2: 131:286357

L61 ANSWER 12 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN
RN 246853-66-7 REGISTRY
ED Entered STN: 09 Nov 1999
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-ethylphenyl)methyl]amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C38 H40 N2 O6 . C2 H F3 O2
SR CA
LC STN Files: CA, CAPLUS

CM 1

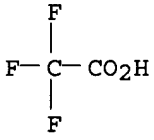
CRN 246853-65-6
CMF C38 H40 N2 O6

Relative stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

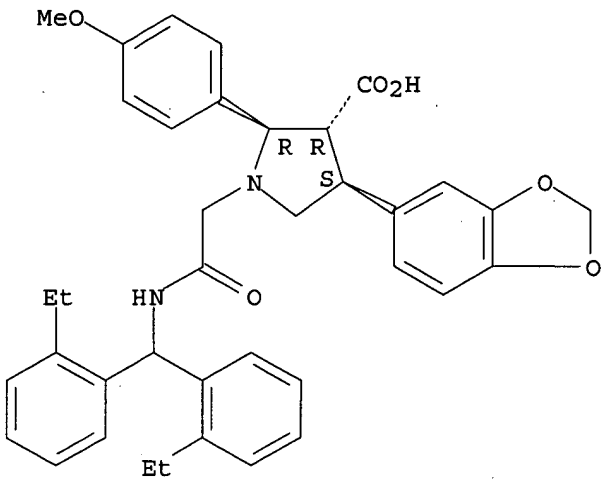


1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:286357

L61 ANSWER 13 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN
RN 246853-65-6 REGISTRY
ED Entered STN: 09 Nov 1999
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-ethylphenyl)methyl]amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C38 H40 N2 O6
CI COM
SR CA

Relative stereochemistry.



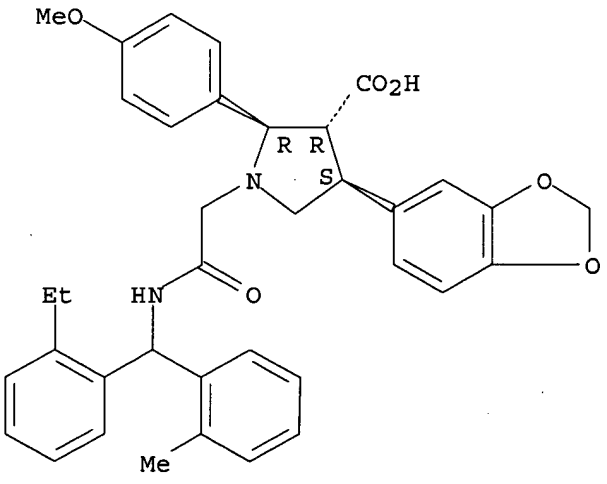
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L61 ANSWER 14 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN
RN 246853-64-5 REGISTRY
ED Entered STN: 09 Nov 1999
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[(2-ethylphenyl)(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C37 H38 N2 O6 . C2 H F3 O2
SR CA
LC STN Files: CA, CAPLUS

CM 1

CRN 246853-63-4
CMF C37 H38 N2 O6

Relative stereochemistry.



CM 2

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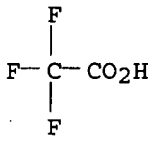
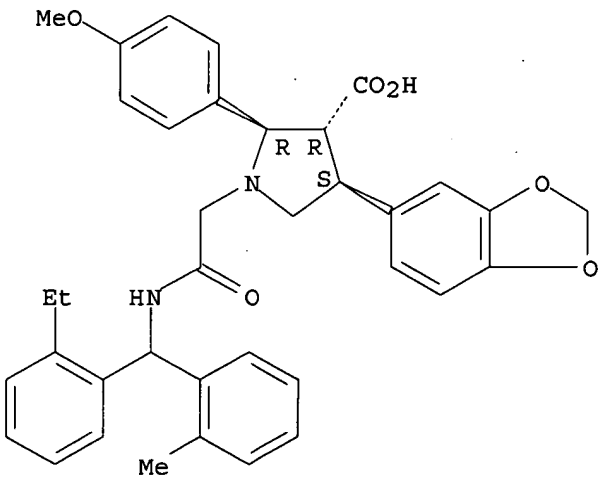


1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:286357

L61 ANSWER 15 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN
RN 246853-63-4 REGISTRY
ED Entered STN: 09 Nov 1999
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[(2-ethylphenyl)(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C37 H38 N2 O6
CI COM
SR CA

Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L61 ANSWER 16 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN
RN 246853-61-2 REGISTRY
ED Entered STN: 09 Nov 1999
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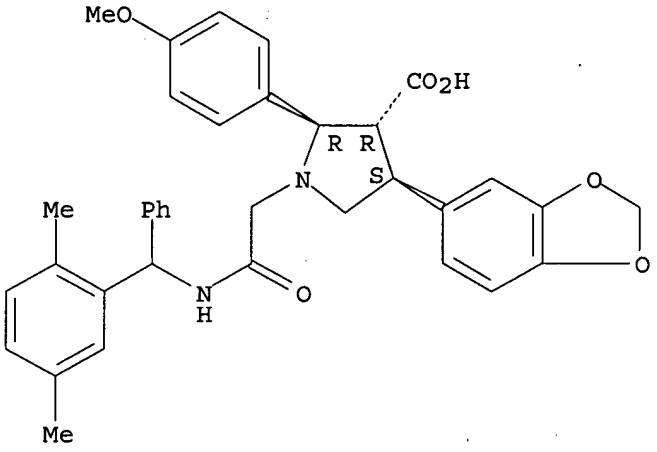
dimethylphenyl)phenylmethyl]amino]-2-oxoethyl]-2-(4-methoxyphenyl)-,
(2R,3R,4S)-rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C36 H36 N2 O6
SR CA
LC STN Files: CA, CAPLUS

Relative stereochemistry.



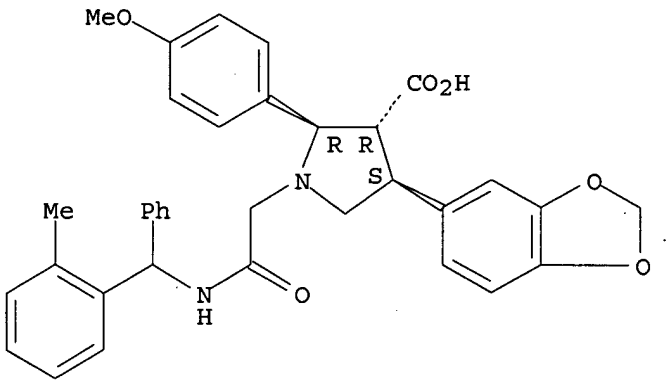
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:286357

L61 ANSWER 17 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN
RN 246853-60-1 REGISTRY
ED Entered STN: 09 Nov 1999
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-2-(4-methoxyphenyl)-
1-[2-[[(2-methylphenyl)phenylmethyl]amino]-2-oxoethyl]-, (2R,3R,4S)-rel-
(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C35 H34 N2 O6
SR CA
LC STN Files: CA, CAPLUS

Relative stereochemistry.



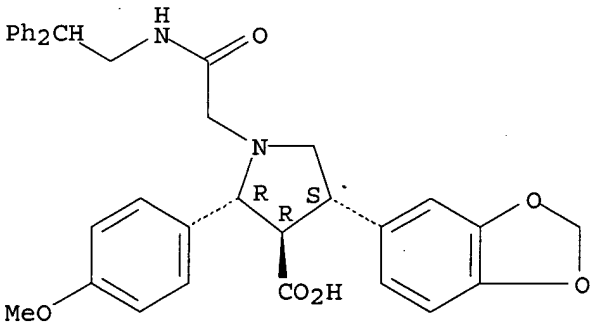
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:286357

L61 ANSWER 18 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN
RN 246853-58-7 REGISTRY
ED Entered STN: 09 Nov 1999
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[(2,2-diphenylethyl)amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C35 H34 N2 O6
SR CA
LC STN Files: CA, CAPLUS

Relative stereochemistry.



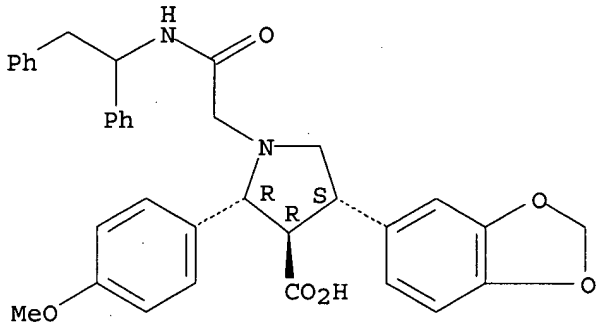
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:286357

L61 ANSWER 19 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN
RN 246853-57-6 REGISTRY
ED Entered STN: 09 Nov 1999
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[(1,2-diphenylethyl)amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C35 H34 N2 O6
SR CA
LC STN Files: CA, CAPLUS

Relative stereochemistry.



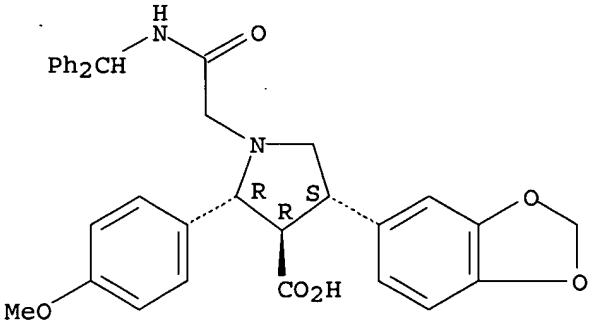
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:286357

L61 ANSWER 20 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN
RN 246853-55-4 REGISTRY
ED Entered STN: 09 Nov 1999
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[(diphenylmethyl)amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C34 H32 N2 O6
SR CA
LC STN Files: CA, CAPLUS

Relative stereochemistry.



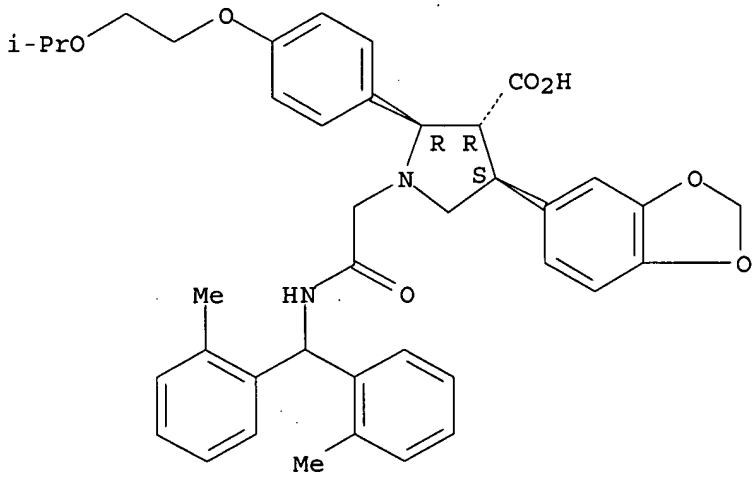
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:286357

L61 ANSWER 21 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN
RN 246853-53-2 REGISTRY
ED Entered STN: 09 Nov 1999
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-[4-[2-(1-methylethoxy)ethoxy]phenyl]-, (2R,3R,4S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C40 H44 N2 O7
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry. Rotation (+).



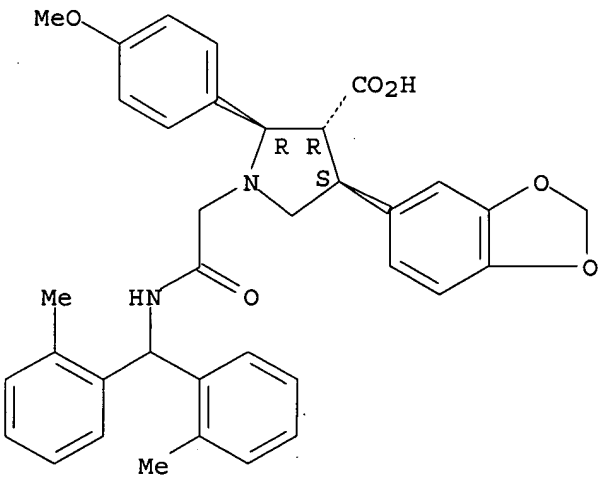
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:286357

L61 ANSWER 22 OF 22 REGISTRY COPYRIGHT 2005 ACS on STN
RN 246853-46-3 REGISTRY
ED Entered STN: 09 Nov 1999
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C36 H36 N2 O6
CI COM
SR CA
LC STN Files: CA, CAPLUS

Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 136:232311

REFERENCE 2: 131:286357

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 15:44:18 ON 28 JUN 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 28 Jun 2005 VOL 143 ISS 1
FILE LAST UPDATED: 27 Jun 2005 (20050627/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> => d all hitstr l65

L65 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:322089 HCAPLUS
DN 141:16897
ED Entered STN: 21 Apr 2004
TI Chemical Function Based Pharmacophore Generation of Endothelin-A Selective Receptor Antagonists
AU Funk, Oliver F.; Kettmann, Viktor; Drimal, Jan; Langer, Thierry
CS Department of Pharmaceutical, Chemistry Institute of Pharmacy, University of Innsbruck, Innsbruck, A-6020, Austria
SO Journal of Medicinal Chemistry (2004), 47(11), 2750-2760
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
CC 1-3 (Pharmacology)
AB Both quant. and qual. chemical function based pharmacophore models of endothelin-A (ETA) selective receptor antagonists were generated by using the two algorithms HypoGen and HipHop, resp., which are implemented in the Catalyst mol. modeling software. The input for HypoGen is a training set of 18 ETA antagonists exhibiting IC50 values ranging between 0.19 nM and 67 μM. The best output hypothesis consists of five features: two hydrophobic (HY), one ring aromatic (RA), one hydrogen bond acceptor (HBA), and one neg. ionizable (NI) function. The highest scoring Hip Hop model consists of six features: three hydrophobic (HY), one ring aromatic (RA), one hydrogen bond acceptor (HBA), and one neg. ionizable (NI). It is the result of an input of three highly active, selective, and structurally diverse ETA antagonists. The predictive power of the quant. model could be approved by using a test set of 30 compds., whose activity values spread over 6 orders of magnitude. The two pharmacophores were tested according to their ability to extract known endothelin antagonists from the 3D mol. structure database of Derwent's World Drug Index. Thereby the main part of selective ETA antagonistic entries was detected by the two hypotheses. Furthermore, the pharmacophores were used to screen the Maybridge database. Six compds. were chosen from the output hit lists for in vitro testing of their ability to displace endothelin-1 from its receptor. Two of these are new potential lead compds. because they are structurally novel and exhibit satisfactory activity in the binding assay.
ST pharmacophore endothelin A receptor binding structure screening drug design; Maybridge database screening algorithm pharmacophore endothelin A receptor antagonist; mol modeling endothelin A receptor antagonist QSAR prediction
IT Computer program
(Catalyst mol. modeling; chemical function bsed pharmacophore generation of endothelin-A selective receptor antagonists)

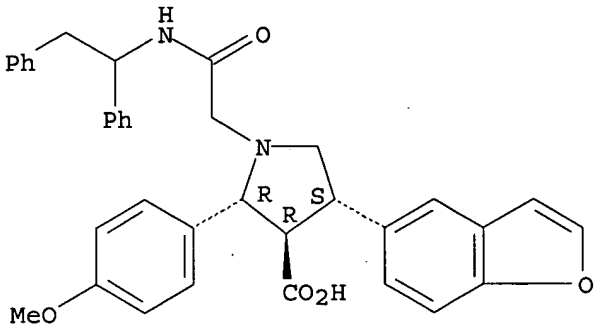
IT Algorithm
(HipHop; chemical function bsed pharmacophore generation of endothelin-A selective receptor antagonists)
IT Algorithm
(HypoGen; chemical function bsed pharmacophore generation of endothelin-A selective receptor antagonists)
IT Databases
(Maybridge; chemical function bsed pharmacophore generation of endothelin-A selective receptor antagonists)
IT Drug design
Drug screening
Molecular modeling
Pharmacophores
QSAR (structure-activity relationship)
(chemical function bsed pharmacophore generation of endothelin-A selective receptor antagonists)
IT Structure-activity relationship
(receptor-binding, endothelin-A; chemical function bsed pharmacophore generation of endothelin-A selective receptor antagonists)
IT Endothelin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type ETA; chemical function bsed pharmacophore generation of endothelin-A selective receptor antagonists)
IT 123626-67-5, Endothelin-1
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(chemical function bsed pharmacophore generation of endothelin-A selective receptor antagonists)
IT 155561-67-4 158692-14-9 173864-15-8 173864-16-9 173937-91-2
173937-92-3 180303-24-6 186021-86-3 186021-94-3 187153-80-6
195704-72-4 195707-32-5 203918-14-3 203918-15-4 203918-19-8
203918-59-6 203919-16-8 203919-21-5 207522-05-2 212480-65-4
237427-20-2 237763-19-8 246853-72-5 366012-89-7 434284-99-8
434285-04-8 434285-10-6 434285-16-2 434285-36-6 434285-42-4
434285-43-5 434285-46-8 677009-36-8 681212-82-8, HTS 00117
681213-04-7, HTS 00155 697767-51-4 697767-52-5 697767-53-6
697767-54-7 697767-55-8 697767-56-9 697767-57-0 697767-58-1
697767-59-2 **697767-60-5** 697767-61-6 697767-62-7
697767-63-8 697767-64-9 697767-65-0 697767-66-1 697767-67-2
697767-68-3 697767-69-4 697767-70-7 697767-71-8 697800-66-1, S 08597
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chemical function bsed pharmacophore generation of endothelin-A selective receptor antagonists)
RE.CNT 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Accelrys Inc; Catalyst, version 4.7
(2) Anon; Derwent World Drug Index 1996
(3) Anon; English philosopher and Franciscan monk William of Ockham P1285
(4) Anon; Ensemble:A New Database Affording a Unique, Integrated View of Drug Information, http://www.prous.com 2001
(5) Arai, H; Nature 1990, V348, P730 HCAPLUS
(6) Balakin, K; J Chem Inf Comput Sci 2002, V42, P1332 HCAPLUS
(7) Barnum, D; J Chem Inf Comput Sci 1996, V36, P563 HCAPLUS
(8) Brooks, B; J Comput Chem 1983, V4, P187 HCAPLUS
(9) Cardillo, C; Hypertension 1999, V33, P753 HCAPLUS
(10) Cramer, R; J Am Chem Soc 1988, V110, P5959 HCAPLUS
(11) de Nucci, G; Proc Natl Acad Sci U S A 1988, V85, P9797 HCAPLUS
(12) Debnath, A; J Med Chem 2002, V45, P41 HCAPLUS
(13) Doherty, A; J Med Chem 1995, V38, P1259 HCAPLUS

(14) Drimal, J; Biology 2000, V55, P299 HCAPLUS
(15) Elliot, J; Endothelin and Its Inhibitors, Chapter 9 2001
(16) Elliott, J; J Med Chem 1994, V37, P1553 HCAPLUS
(17) Fischer, R; The Design of Experiments, 8th ed, Chapter II 1966
(18) Hirashima, A; Bioorg Med Chem 1999, V7, P1437 HCAPLUS
(19) Inoue, A; Proc Natl Acad Sci U S A 1989, V86, P2863 HCAPLUS
(20) Ishikawa, K; Proc Natl Acad Sci U S A 1994, V91, P4892 HCAPLUS
(21) Ishizuka, N; J Med Chem 2002, V45, P2041 HCAPLUS
(22) Jae, H; J Med Chem 1997, V40, P3217 HCAPLUS
(23) Kalra, P; Int J Cardiol 2002, V85, P195
(24) Kaminski, J; J Med Chem 1997, V40, P4103 HCAPLUS
(25) Karki, R; Eur J Med Chem 2001, V36, P147 HCAPLUS
(26) Kiowski, W; Lancet 1995, V346, P732 MEDLINE
(27) Krovat, E; J Med Chem 2003, V46, P716 HCAPLUS
(28) Krum, H; N Engl J Med 1998, V338, P784 HCAPLUS
(29) Kukkola, P; Bioorg Med Chem Lett 2001, V11, P1737 HCAPLUS
(30) Kurogi, Y; J Med Chem 2001, V44, P2304 HCAPLUS
(31) Langer, T; J Mol Struct:THEOCHEM 2000, V503, P59 HCAPLUS
(32) Li, H; Pharmacophore Perception, Development and Use in Drug Design 2000
(33) Lipinski, C; Adv Drug Dev Rev 1997, V23, P3 HCAPLUS
(34) Liu, G; J Med Chem 1998, V41, P3261 HCAPLUS
(35) Liu, G; J Med Chem 1999, V42, P3679 HCAPLUS
(36) Lopez-Rodriguez, M; Bioorg Med Chem Lett 2000, V10, P1097 HCAPLUS
(37) Maloney, J; Curr Opin Pulm Med 2003, V9, P139
(38) Maybridge Chemical Company; The Maybridge Database 2001
(39) Mederski, W; Bioorg Med Chem Lett 1999, V9, P619 HCAPLUS
(40) Moreland, S; Biochem Biophys Res Commun 1992, V184, P100 HCAPLUS
(41) Nishikibe, M; Am Soc Pharm Exp Ther 1999, V283, P1262
(42) Ohlstein, E; Eur J Pharmacol 1992, V225, P347 HCAPLUS
(43) Ohnishi, M; Cardiovasc Res 1998, V39, P617 HCAPLUS
(44) Omoshile, O; Pharmacophore Perception, Development and Use in Drug Design 2000
(45) Palomer, A; J Med Chem 2002, V45, P1402 HCAPLUS
(46) Panek, R; Biochem Biophys Res Commun 1992, V183, P572 HCAPLUS
(47) Patt, W; J Med Chem 1997, V40, P1063 HCAPLUS
(48) Patt, W; J Med Chem 1999, V42, P2162 HCAPLUS
(49) Saavedra, J; InPlot A Nonlinear Least-Squares Curve-Fitting Program, version 4.03 1992
(50) Saeki, T; Biochem Biophys Res Commun 1991, V179, P286 HCAPLUS
(51) Sakurai, T; Trends Pharmacol Sci 1992, V13, P103 HCAPLUS
(52) Singh, J; J Med Chem 2002, V45, P2988 HCAPLUS
(53) Smellie, A; J Comput Chem 1995, V16, P171 HCAPLUS
(54) Stewart, D; Ann Intern Med 1991, V114, P464 MEDLINE
(55) Stewart, D; Can J Cardiol 1998, Suppl D, P11D
(56) Sutsch, G; Circulation 1998, V98, P2262 HCAPLUS
(57) Tafi, A; J Med Chem 2002, V45, P2720 HCAPLUS
(58) Takayanagi, R; FEBS Lett 1991, V282, P103 HCAPLUS
(59) Tasker, A; J Med Chem 1997, V40, P322 HCAPLUS
(60) Verhaar, M; Circulation 1998, V97, P752 HCAPLUS
(61) Von Geldern, T; J Med Chem 1999, V42, P3668 HCAPLUS
(62) Warner, T; J Cardiovasc Pharmacol 1989, V13, P85
(63) Webb, M; Biochemistry 1996, V35, P2548 HCAPLUS
(64) Winn, M; J Med Chem 1996, V39, P1039 HCAPLUS
(65) Wu, C; Expert Opin Ther Pat 2000, V10, P1653 HCAPLUS
(66) Zolk, O; Circulation 1999, V99, P2118 HCAPLUS

IT **697767-60-5**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chemical function bsed pharmacophore generation of endothelin-A selective receptor antagonists)

RN 697767-60-5 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 4-(5-benzofuranyl)-1-[2-[(1,2-diphenylethyl)amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



=> d all hitstr l64 tot

L64 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:171682 HCAPLUS
DN 136:232311
ED Entered STN: 08 Mar 2002
TI Preparation of 4-benzoheterocyclyl-1-aminocarbonylmethylpyrrolidine-3-carboxylic acid derivatives as endothelin antagonists
IN **Winn, Martin; Boyd, Steven A.; Hutchins, Charles W.; Hwan-Soo, Jae; Tasker, Andrew S.; Von Geldern, Tomas W.; Kester, Jeffrey; Sorensen, Bryan K.; Szczepankiewicz, Bruce G.; Henry, Kenneth; Liu, Gang; Wittenberger, Steven J.; King, Steven A.; Janus, Todd J.; Padley, Robert J.**
PA **Abbott** Laboratories, USA
SO PCT Int. Appl., 817 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-4025
ICS A61P009-12; C07D405-04
CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002017912	A1	20020307	WO 2001-US27220	20010831 <--

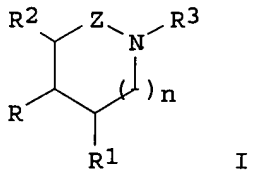
W: CA, JP, MX
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR

PRAI US 2000-653563 A 20000831 <--

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2002017912	ICM	A61K031-4025
	ICS	A61P009-12; C07D405-04
WO 2002017912	ECLA	C07D405/04+317+207 <--

OS MARPAT 136:232311
GI



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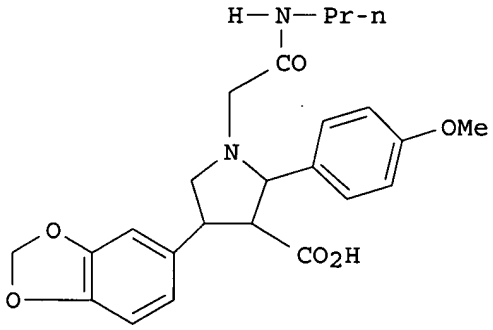

II

AB Title compds. [I; n = 0; Z = CH2; R = CO2H; R1 = alkoxyaryl, alkoxyalkoxyaryl, heterocyclylalkyl; R2 = 1,3-benzodioxyl, 4-benzofuranyl, 5-indanyl; R3 = R4R5CO; R4 = R6R7N, R8R9NNH; R5 = methylene; one of R6, R7 is H, the other is arylalkyl, diarylalkyl; one of R8, R9 is alkyl, the other is aryl] stereoisomers, and pharmaceutically acceptable salts are prepared as endothelin antagonists. Thus, the title compound II was prepared from Et (4-methoxybenzoyl)acetate, 5-(2-nitrovinyl)-1,3-benzodioxol, ethyldiisopropylamine, and N-Pr bromoacetamide and was in vitro tested for binding effect to the endothelin receptor and the determination of title compound as functional ET antagonist.

ST benzodioxolyl aminocarbonylmethylpyrrolidinecarboxylic acid prepn endothelin antagonist; oxopyrimidinylethyl benzodioxolyl aminocarbonylmethylpyrrolidinecarboxylic acid prepn endothelin antagonist; indanyl aminocarbonylmethylpyrrolidinecarboxylic acid prepn endothelin antagonist; benzofuranyl aminocarbonylmethylpyrrolidinecarboxylic acid prepn endothelin antagonist

IT Endothelin receptors
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(preparation of 4-benzoheterocyclyl-1-aminocarbonylmethylpyrrolidine-3-carboxylic acid derivs. as endothelin antagonists)

IT 116243-73-3, Endothelin
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(preparation of 4-benzoheterocyclyl-1-aminocarbonylmethylpyrrolidine-3-

carboxylic acid derivs. as endothelin antagonists)

IT 195708-83-9P
RL: BYP (Byproduct); SPN (Synthetic preparation); PREP (Preparation)
(preparation of 4-benzoheterocyclyl-1-aminocarbonylmethylpyrrolidine-3-carboxylic acid derivs. as endothelin antagonists)

IT 173864-16-9P 178608-45-2P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 4-benzoheterocyclyl-1-aminocarbonylmethylpyrrolidine-3-carboxylic acid derivs. as endothelin antagonists)

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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)
(preparation of 4-benzoheterocyclyl-1-aminocarbonylmethylpyrrolidine-3-carboxylic acid derivs. as endothelin antagonists)

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403657-02-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 4-benzoheterocyclyl-1-aminocarbonylmethylpyrrolidine-3-carboxylic acid derivs. as endothelin antagonists)

IT 66-77-3, Naphthalene-1-carboxaldehyde 66-99-9, Naphthalene-2-carboxaldehyde 75-64-9, reactions 78-39-7, Triethyl orthoacetate 79-03-8, Propionyl chloride 79-30-1, Isobutyryl chloride 94-02-0, Ethyl benzoylacetate 96-48-0, γ-Butyrolactone 98-10-2, Benzenesulfonamide 99-66-1, 2-Propylpentanoic acid 100-06-1 100-52-7, Benzaldehyde, reactions 100-69-6, 2-Vinylpyridine 103-71-9, Phenyl isocyanate, reactions 106-41-2, 4-Bromophenol 107-03-9, 1-Propanethiol 107-10-8, Propylamine, reactions 107-86-8, 3-Methyl-2-butenal 107-87-9, 2-Pentanone 108-10-1, 4-Methyl-2-pentanone 109-73-9, n-Butylamine, reactions 109-90-0, Ethyl isocyanate 111-36-4, Butyl isocyanate 111-92-2, Dibutylamine 120-14-9, 3,4-Dimethoxybenzaldehyde 120-57-0, Piperonal 123-08-0, 4-Hydroxybenzaldehyde 123-11-5, 4-Methoxybenzaldehyde, reactions 123-19-3, 4-Heptanone 141-75-3, Butyryl chloride 141-97-9, Ethyl

acetoacetate 142-84-7, Dipropylamine 144-48-9, Iodoacetamide 328-38-1, D-Leucine 455-88-9, 2-Fluoro-5-nitrotoluene 455-91-4 459-46-1, 4-Fluorobenzyl bromide 459-57-4, 4-Fluorobenzaldehyde 496-16-2, 2,3-Dihydrobenzofuran 527-69-5, 2-Furoyl chloride 541-41-3, Ethyl chloroformate 542-69-8, 1-Iodobutane 574-98-1 590-86-3, Isovaleraldehyde 591-20-8, 3-Bromophenol 591-31-1, 3-Methoxybenzaldehyde 592-55-2, 2-Bromoethyl ethyl ether 598-72-1, 2-Bromopropanoic acid 613-45-6, 2,4-Dimethoxybenzaldehyde 615-20-3, 2-Chlorobenzothiazole 693-07-2, 2-Chloroethyl ethyl sulfide 1018-97-9, 2,2'-Dimethylbenzophenone 1126-78-9, N-Butyl aniline 1191-99-7, 2,3-Dihydrofuran 1196-70-9, Indole-6-carboxaldehyde 1877-77-6, 3-Aminobenzyl alcohol 2032-35-1, Bromoacetaldehyde diethyl acetal 2386-60-9, 1-Butanesulfonyl chloride 2859-68-9, 3-(2-Pyridyl)-propanol 3085-68-5, N,N-Diallyl acrylamide 3179-10-0, 4-(2-Nitrovinyl)anisole 3182-95-4, (S)-Phenylalaninol 3249-68-1, Ethyl butyrylacetate 3840-30-0, 3,4,5-Trimethoxybenzyl chloride 3934-20-1, 2,4-Dichloropyrimidine 4595-60-2, 2-Bromopyrimidine 5292-43-3, tert-Butyl bromoacetate 5395-67-5, N-Propyl bromoacetamide 5416-93-3, 4-Methoxyphenyl isocyanate 5695-63-6, 2-Bromomethyl-1,3-dioxane 5780-07-4, 5-Methoxypiperonal 6291-85-6, 3-Ethoxypropylamine 7087-68-5 7152-15-0, Ethyl isobutyrylacetate 7663-76-5 10035-16-2, Benzofuran-5-carboxaldehyde 10147-36-1, Propylsulfonyl chloride 10147-37-2, 2-Propanesulfonyl chloride 10554-65-1, 6-(2-Nitrovinyl)-1,4-benzodioxane 13358-73-1, Dibutylcarbamoyl chloride 15159-40-7, 4-Morpholinocarbonyl chloride 18495-25-5, 1-Bromo-2-hexyne 20261-68-1, 1-Chloro-2-hexanone 23590-03-6, N,N-Dibutyl glycine 24074-26-8, Diisopropyl(ethoxycarbonylmethyl)phosphonate 34036-07-2, 3,4-Difluorobenzaldehyde 38945-21-0, O-Allylhydroxylamine hydrochloride 42149-74-6, 2-Chloroethyl propyl ether 51445-11-5 51932-70-8, Indan-4-carboxaldehyde 54149-17-6, 2-(2-Methoxyethoxy)ethyl bromide 55745-70-5, 2,3-Dihydrobenzofuran-5-carboxaldehyde 63131-29-3, Methyl (4-fluorobenzoyl)acetate 73873-61-7, trans-4-Methoxycyclohexane carboxylic acid 81581-27-3, Ethyl (1,3-benzodioxol-5-ylcarbonyl)acetate 90719-32-7, (S)-4-Benzyl-2-oxazolidinone 101498-88-8, Ethyl (4-tert-butylbenzoyl)acetate 110874-83-4, Methyl 3-oxo-6-octenoate 116169-12-1, Ethyl 3,3-dimethylhexanoate 134414-16-7, N-Butyl-N-methyl bromoacetamide 158692-25-2 178609-50-2 178609-64-8, N-Methyl-N-propyl bromoacetamide 178609-65-9, Ethyl (4-methoxy-2-(methoxymethoxybenzoyl)acetate 178609-66-0, N-(3,4-Dimethoxybenzyl) 2-bromoacetamide 178609-67-1 178609-68-2 220584-69-0 220584-95-2 288309-52-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 4-benzoheterocyclyl-1-aminocarbonylmethylpyrrolidine-3-carboxylic acid derivs. as endothelin antagonists)

IT 111-75-1P, N-Butyl-N-(2-hydroxyethyl)amine 452-69-7P, 4-Fluoro-3-methylaniline 589-55-9P, 4-Heptanol 937-33-7P 1485-00-3P 1589-35-1P, trans-5-Methylhex-2-en-1-ol 2881-83-6P 4325-82-0P, 4-Methyl-3-penten-2-ol 4543-95-7P 5326-87-4P, N-Phenylbromoacetamide 6303-18-0P, 1-Pentanesulfonyl chloride 15197-75-8P, 2-Pyridinepropanoic acid 15896-78-3P 17664-93-6P, D-Leucine benzyl ester tosylate 22568-48-5P 24066-72-6P 24642-84-0P 25560-11-6P 30084-91-4P, Indan-5-carboxaldehyde 34993-63-0P 36171-18-3P 40124-27-4P, N,N-Dibutylbromoacetamide 41692-47-1P, Ethyl 3-methylhexanoate 42042-67-1P, N-Butyl-4-hydroxybutyramide 67764-22-1P 77191-38-9P 81042-10-6P 89532-73-0P, 3-(1-Pyrazolyl)-propionic acid 90843-31-5P, 5-Acetyl-2,3-dihydrobenzofuran 95333-13-4P, Benzofuran-4-carboxaldehyde 100366-94-7P 103335-72-4P 123297-88-1P, Benzofuran-6-carboxaldehyde 149673-73-4P 173864-36-3P 173864-45-4P 173864-46-5P 173864-47-6P 173864-48-7P 173937-93-4P 178609-16-0P 178609-18-2P 178609-21-7P 178609-22-8P 178609-24-0P 178609-26-2P, 1-Chloro-3-propyl-2-hexanone

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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 4-benzoheterocyclyl-1-aminocarbonylmethylpyrrolidine-3-carboxylic acid derivs. as endothelin antagonists)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

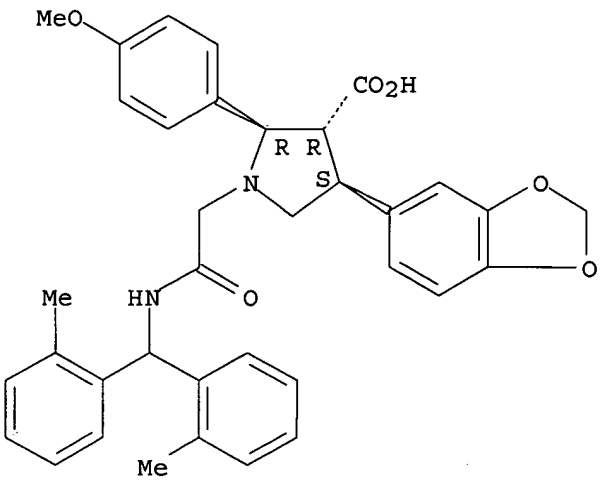
(1) Abbott Lab; WO 9606095 A 1996 HCAPLUS
(2) Abbott Lab; WO 9730045 A 1997 HCAPLUS
(3) Abbott Lab; WO 9730046 A 1997 HCAPLUS
(4) Liu, G; J MED CHEM 1999, V42(18), P3679 HCAPLUS

IT **246853-46-3P 246853-81-6P 246853-83-8P**
403614-24-4P 403614-26-6P 403614-29-9P
403614-30-2P 403614-31-3P 403614-32-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 4-benzoheterocyclyl-1-aminocarbonylmethylpyrrolidine-3-carboxylic acid derivs. as endothelin antagonists)

RN 246853-46-3 HCAPLUS

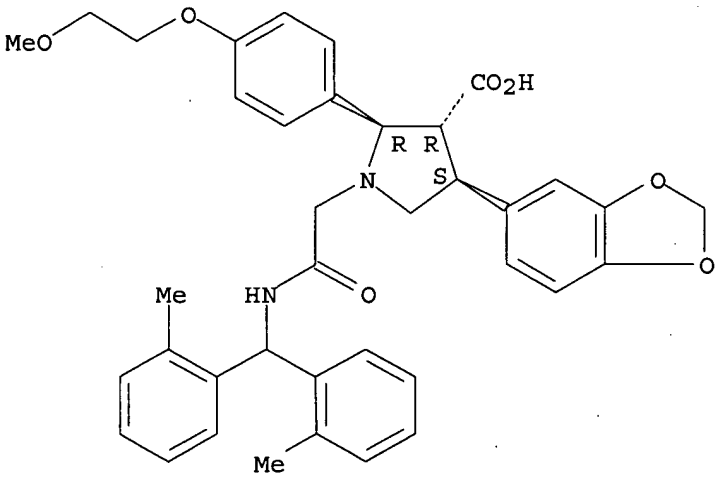
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



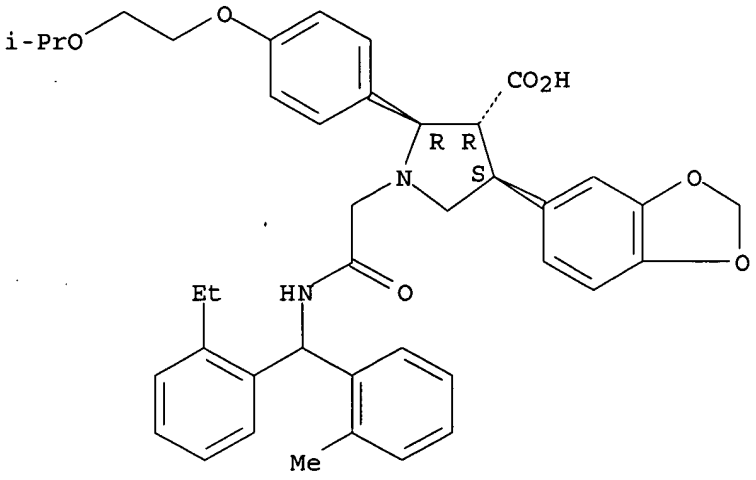
RN 246853-81-6 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-[4-(2-methoxyethoxy)phenyl]-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 246853-83-8 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[(2-ethylphenyl)(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-[4-[2-(1-methylethoxy)ethoxy]phenyl]-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

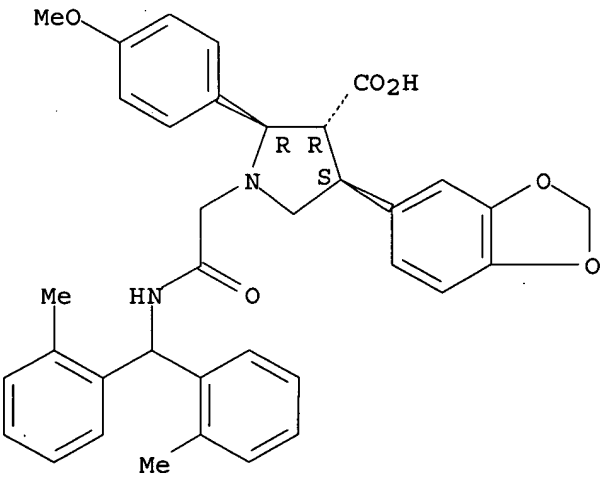


RN 403614-24-4 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel-, trifluoroacetate (5:2) (9CI) (CA INDEX NAME)

CM 1

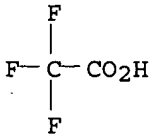
CRN 246853-46-3
CMF C36 H36 N2 O6

Relative stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

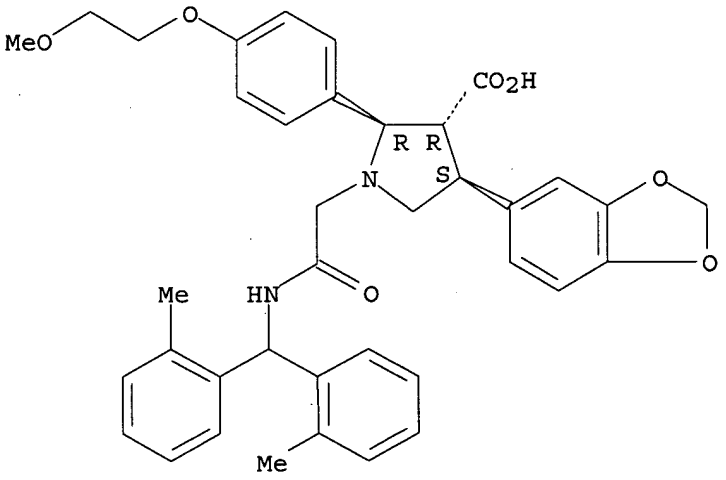


RN 403614-26-6 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-[4-(2-methoxyethoxy)phenyl]-, (2R,3R,4S)-rel-, trifluoroacetate (5:1) (9CI) (CA INDEX NAME)

CM 1

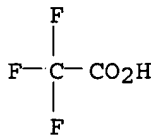
CRN 246853-81-6
CMF C38 H40 N2 O7

Relative stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

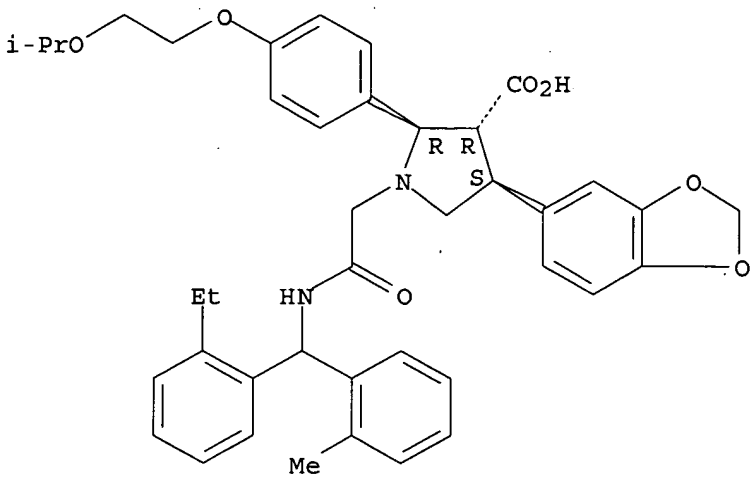


RN 403614-29-9 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[(2-ethylphenyl)(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-[4-[2-(1-methylethoxy)ethoxy]phenyl]-, (2R,3R,4S)-rel-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

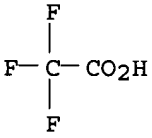
CRN 246853-83-8
CMF C41 H46 N2 O7

Relative stereochemistry.



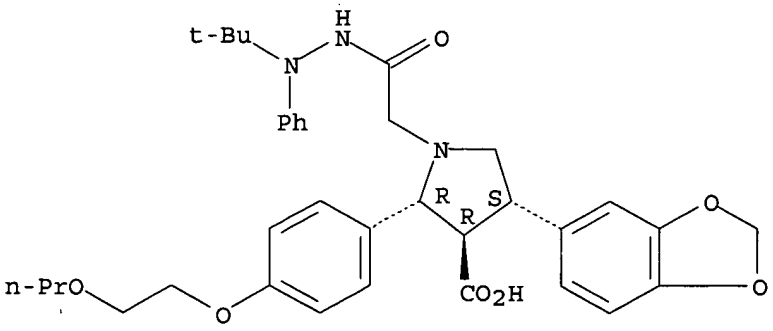
CM 2

CRN 76-05-1
CMF C2 H F3 O2



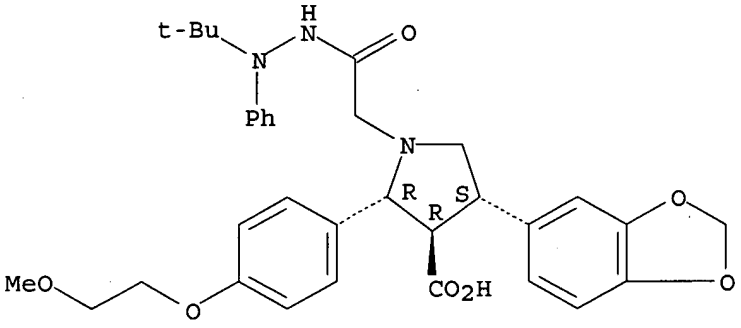
RN 403614-30-2 HCAPLUS
CN 1-Pyrrolidineacetic acid, 4-(1,3-benzodioxol-5-yl)-3-carboxy-2-[4-(2-propoxyethoxy)phenyl]-, α-[2-(1,1-dimethylethyl)-2-phenylhydrazide], (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 403614-31-3 HCAPLUS
CN 1-Pyrrolidineacetic acid, 4-(1,3-benzodioxol-5-yl)-3-carboxy-2-[4-(2-methoxyethoxy)phenyl]-, α-[2-(1,1-dimethylethyl)-2-phenylhydrazide], (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

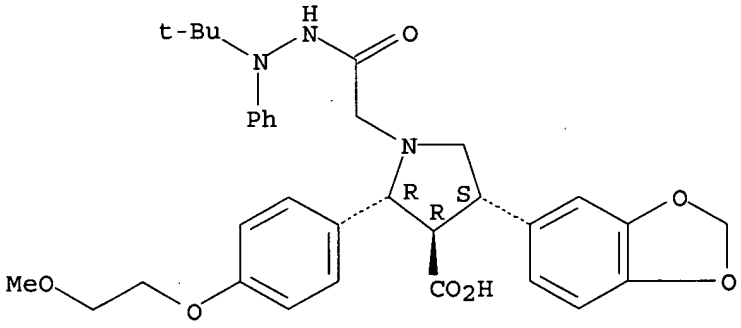


RN 403614-32-4 HCAPLUS
CN 1-Pyrrolidineacetic acid, 4-(1,3-benzodioxol-5-yl)-3-carboxy-2-[4-(2-methoxyethoxy)phenyl]-, α-[2-(1,1-dimethylethyl)-2-phenylhydrazide], (2R,3R,4S)-rel-, monoacetate (9CI) (CA INDEX NAME)

CM 1

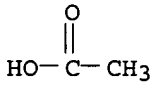
CRN 403614-31-3
CMF C33 H39 N3 O7

Relative stereochemistry.

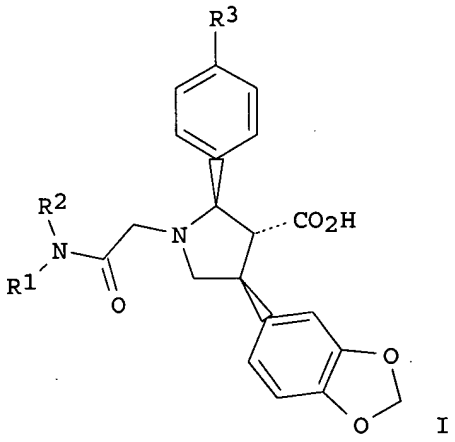


CM 2

CRN 64-19-7
CMF C2 H4 O2



L64 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:510837 HCAPLUS
DN 131:286357
ED Entered STN: 18 Aug 1999
TI Design, Synthesis, and Activity of a Series of Pyrrolidine-3-carboxylic Acid-Based, Highly Specific, Orally Active ETB Antagonists Containing a Diphenylmethylamine Acetamide Side Chain
AU **Liu, Gang**; Kozmina, Natasha S.; **Winn, Martin**; **von Geldern, Thomas W.**; Chiou, William J.; Dixon, Douglas B.; Nguyen, Bach; Marsh, Kennan C.; Opgenorth, Terry J.
CS Metabolic Disease Research and Drug Analysis Department Pharmaceutical Products Division, **Abbott** Laboratories, **Abbott** Park, IL, 60064-6098, USA
SO Journal of Medicinal Chemistry (1999), 42(18), 3679-3689
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
CC 27-10 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
GI



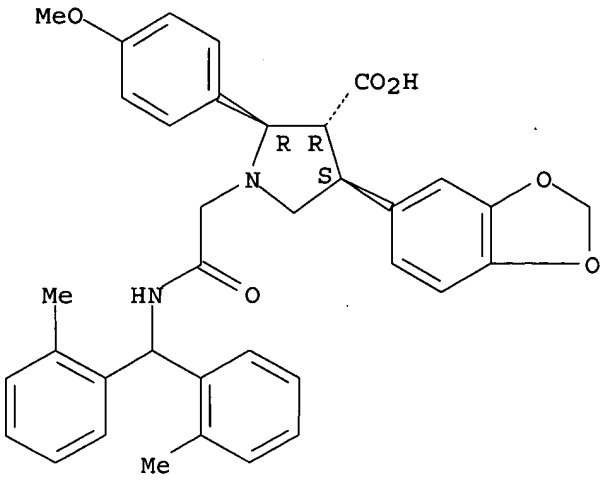
I

AB The endothelin (ET)-B receptor subtype is expressed on vascular endothelial and smooth muscle cells and mediates both vasodilation and vasoconstriction. On the basis of the pharmacophore of the previously reported ETA-specific antagonist I (R1 = R2 = n-Bu; R3 = MeO)(ABT-627), we are reporting the discovery of a novel series of highly specific, orally active ETB receptor antagonists. Replacing the dibutylaminoacetamide group of I with a diphenylmethylaminoacetamide group resulted in antagonist I (R1 = (C6H5)2CH; R2 = H; R3 = MeO) with a complete reversal of receptor specificity. Structure-activity relationship studies revealed that ortho-alkylation of the Ph rings could further increase ETB affinity and also boost the ETA/ETB activity ratio of the resulting antagonists. A similar antagonism selectivity profile could also be achieved when one of the Ph rings of the acetamide side chain was replaced with an alkyl group, preferably a tert-Bu group I [R1 = C6H5(t-Bu)CH; R2 = H; R3 = MeO]. Combining these features with modification of the 2-aryl group of the pyrrolidine core, we have identified a potent antagonist I [R1 = (2-MeC6H4)2CH; R2 = H; R3 = MeOCH2CH2O](A-308165) with over 27 000-fold selectivity favoring the ETB receptor and an acceptable pharmacokinetic

profile (F = 24%) in rats.
ST pyrrolidinecarboxylic acid prepn endothelin B antagonist; endothelin B antagonist structure activity relationship
IT Endothelin receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(ETA; preparation, activity, and structure activity relationship of pyrrolidine-3-carboxylic acid-based ETB antagonists)
IT Endothelin receptors
RL: SPN (Synthetic preparation); PREP (Preparation)
(ETB, antagonist; preparation, activity, and structure activity relationship of pyrrolidine-3-carboxylic acid-based ETB antagonists)
IT Endothelin receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(ETB; preparation, activity, and structure activity relationship of pyrrolidine-3-carboxylic acid-based ETB antagonists)
IT Structure-activity relationship
(endothelin receptor-binding; preparation, activity, and structure activity relationship of pyrrolidine-3-carboxylic acid-based ETB antagonists)
IT **246853-46-3P 246853-53-2P 246853-55-4P**
246853-56-5P **246853-57-6P 246853-58-7P** 246853-59-8P
246853-60-1P 246853-61-2P 246853-64-5P
246853-66-7P 246853-67-8P 246853-68-9P 246853-69-0P
246853-70-3P 246853-71-4P 246853-72-5P 246853-73-6P 246853-74-7P
246853-75-8P 246853-76-9P 246853-77-0P 246853-80-5P
246853-81-6P 246853-82-7P 246853-83-8P
246853-85-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, activity, and structure activity relationship of pyrrolidine-3-carboxylic acid-based ETB antagonists)
IT 246853-50-9P
RL: PUR (Purification or recovery); PREP (Preparation)
(preparation, activity, and structure activity relationship of pyrrolidine-3-carboxylic acid-based ETB antagonists)
IT 246853-51-0P
RL: PUR (Purification or recovery); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(preparation, activity, and structure activity relationship of pyrrolidine-3-carboxylic acid-based ETB antagonists)
IT 100-09-4 1018-97-9, 2,2'-Dimethylbenzophenone 1485-00-3 27890-92-2
246853-48-5 246853-78-1 246853-79-2 246853-84-9 246853-86-1
246853-87-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation, activity, and structure activity relationship of pyrrolidine-3-carboxylic acid-based ETB antagonists)
IT 2881-83-6P 173864-45-4P 173864-47-6P 218271-43-3P 246853-44-1P
246853-45-2P 246853-47-4P 246853-49-6P 246853-54-3P 246853-88-3P
246853-89-4P 246853-90-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, activity, and structure activity relationship of pyrrolidine-3-carboxylic acid-based ETB antagonists)
IT 108714-78-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, biol. activity, and structure activity relationship of pyrrolidine-3-carboxylic acid-based ETB antagonists)

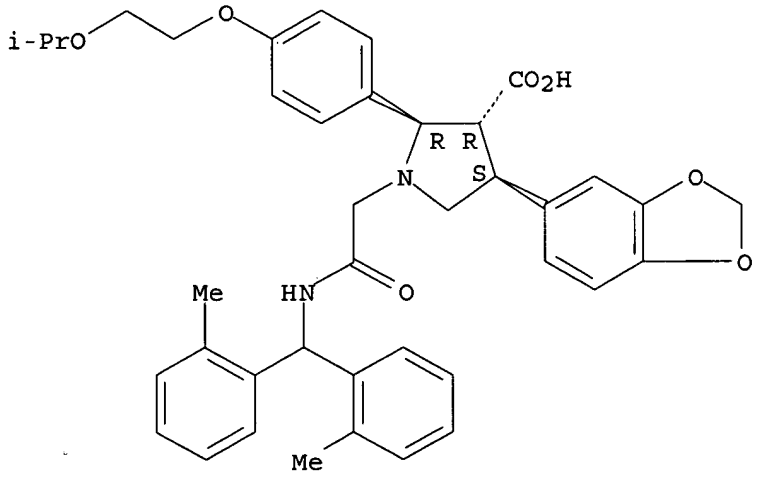
RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Arai, H; Nature 1990, V348, P730 HCAPLUS
(2) Balwierczak, J; J Cardiovasc Pharmacol 1995, V26(Suppl 3), PS393
(3) Berliner, E; J Am Chem Soc 1950, V72, P222 HCAPLUS
(4) Breu, V; FEBS 1996, V383, P37 HCAPLUS
(5) Brooks, D; Angew Chem Int Ed Engl 1979, V18, P72
(6) Burke, S; J Cardiovasc Pharmacol 1997, V30, P33 HCAPLUS
(7) Chan, M; Bioorg Med Chem 1998, V6, P2301
(8) Chen, S; J Cardiovasc Pharmacol 1997, V29, P713 HCAPLUS
(9) Gray, G; Am J Physiol 1994, V266, PH959 HCAPLUS
(10) Harrison, V; Br J Pharmacol 1992, V105, P511 HCAPLUS
(11) Hatt, H; J Chem Soc 1929, P1623 HCAPLUS
(12) Henry, P; Br J Pharmacol 1993, V110, P435 HCAPLUS
(13) Inoue, A; Proc Natl Acad Sci USA 1989, V86, P2863 HCAPLUS
(14) Ishikawa, K; Proc Natl Acad Sci USA 1994, V91, P4892 HCAPLUS
(15) Jae, H; J Med Chem 1997, V40, P3217 HCAPLUS
(16) Kiowski, W; Lancet 1995, V346, P732 MEDLINE
(17) Krapcho, A; Organic Synthesis 1967, V47, P20
(18) Liu, G; J Med Chem 1998, V41, P3261 HCAPLUS
(19) Morishita, Y; J Antibiot 1994, V47, P269 HCAPLUS
(20) Opgenorth, T; Adv Pharmacol (San Diego) 1995, V6, P1
(21) Pollock, D; Ren Fail 1997, V19, P753 HCAPLUS
(22) Sakurai, T; Nature 1990, V348, P732 HCAPLUS
(23) Shetty, S; Biochem Biophys Res Commun 1993, V191, P45
(24) Strachan, F; Hypertension 1999, V33, P581 HCAPLUS
(25) Takayanagi, R; FEBS Lett 1991, V282, P103 HCAPLUS
(26) Underwood, D; J Pharmacol Exp Ther 1997, V283, P1130 HCAPLUS
(27) Vitola, J; J Cardiovasc Pharmacol 1996, V28, P774 HCAPLUS
(28) von Geldern, T; J Med Chem 1999, V42, PXXX
(29) Warner, T; J Cardiovasc Pharmacol 1989, V13(Suppl 5), PS85
(30) Weaver, W; J Am Chem Soc 1947, V69, P515 HCAPLUS
(31) Winn, M; J Med Chem 1996, V39, P1039 HCAPLUS
(32) Yanigasawa, M; Nature 1988, V332, P411
IT **246853-46-3P 246853-53-2P 246853-55-4P**
246853-57-6P 246853-58-7P 246853-60-1P
246853-61-2P 246853-64-5P 246853-66-7P
246853-81-6P 246853-82-7P 246853-83-8P
246853-85-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, activity, and structure activity relationship of pyrrolidine-3-carboxylic acid-based ETB antagonists)
RN 246853-46-3 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



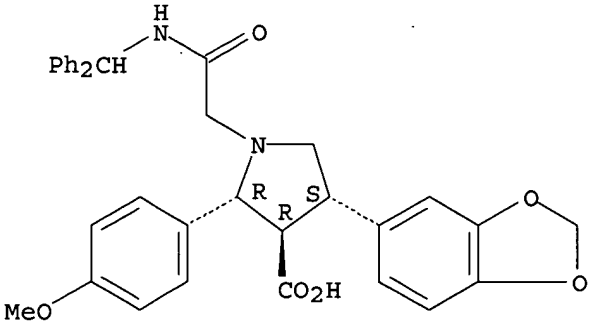
RN 246853-53-2 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-[4-[2-(1-methylethoxy)ethoxy]phenyl]-, (2R,3R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 246853-55-4 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[(diphenylmethyl)amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



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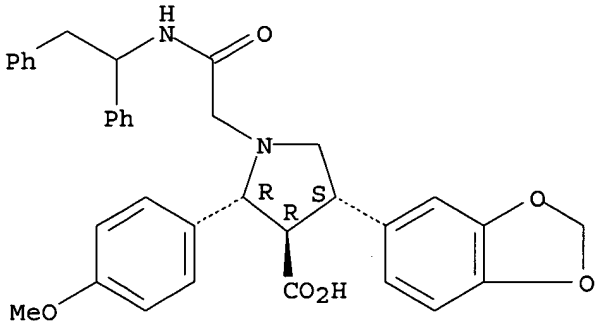
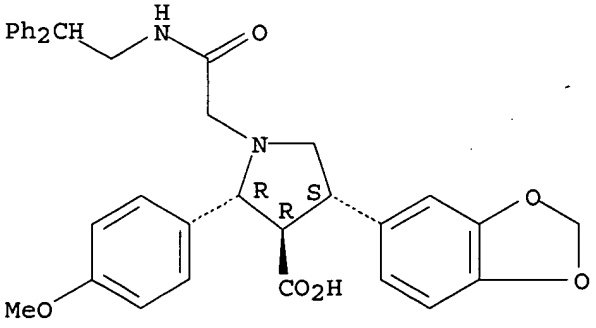
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[(1,2-diphenylethyl)amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 246853-58-7 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[(2,2-diphenylethyl)amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

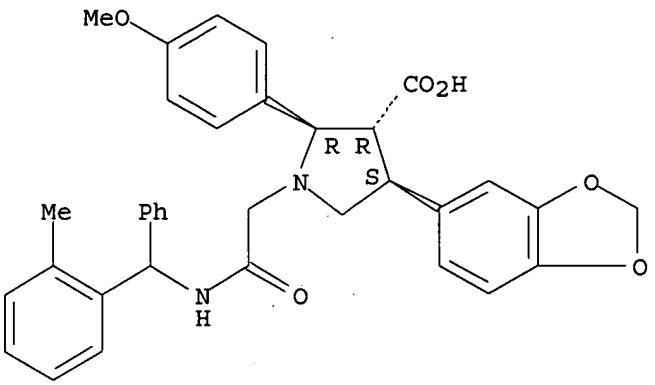
Relative stereochemistry.



RN 246853-60-1 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-2-(4-methoxyphenyl)-1-[2-[[(2-methylphenyl)phenylmethyl]amino]-2-oxoethyl]-, (2R,3R,4S)-rel-

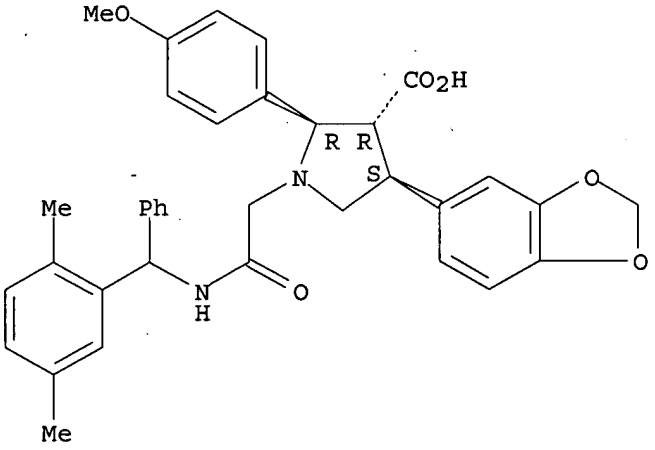
(9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 246853-61-2 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[(2,5-dimethylphenyl)phenylmethyl]amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

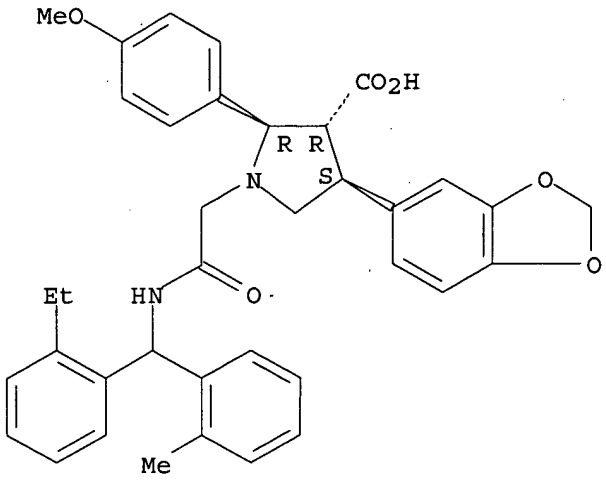


RN 246853-64-5 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[(2-ethylphenyl)(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

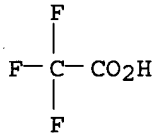
CRN 246853-63-4
CMF C37 H38 N2 O6

Relative stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

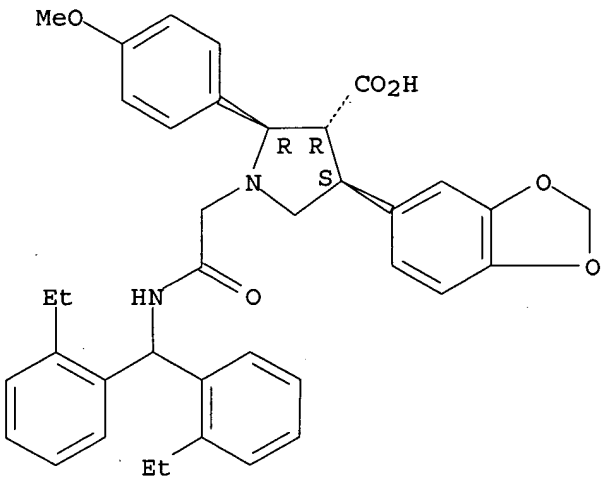


RN 246853-66-7 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-ethylphenyl)methyl]amino]-2-oxoethyl]-2-(4-methoxyphenyl)-, (2R,3R,4S)-rel-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

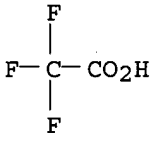
CRN 246853-65-6
CMF C38 H40 N2 O6

Relative stereochemistry.



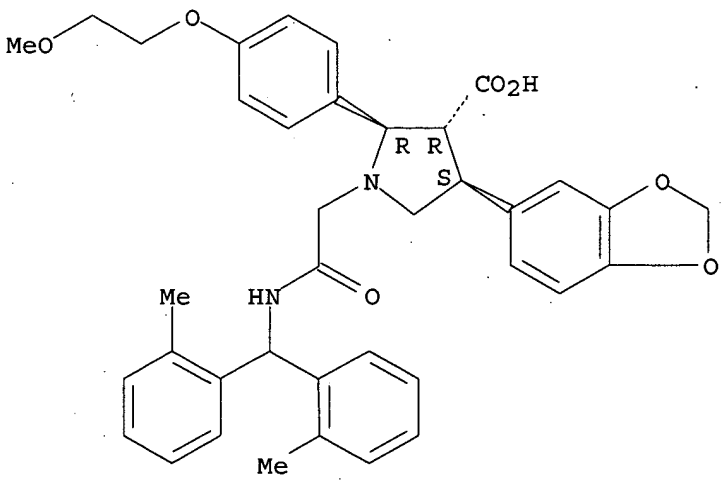
CM 2

CRN 76-05-1
CMF C2 H F3 O2



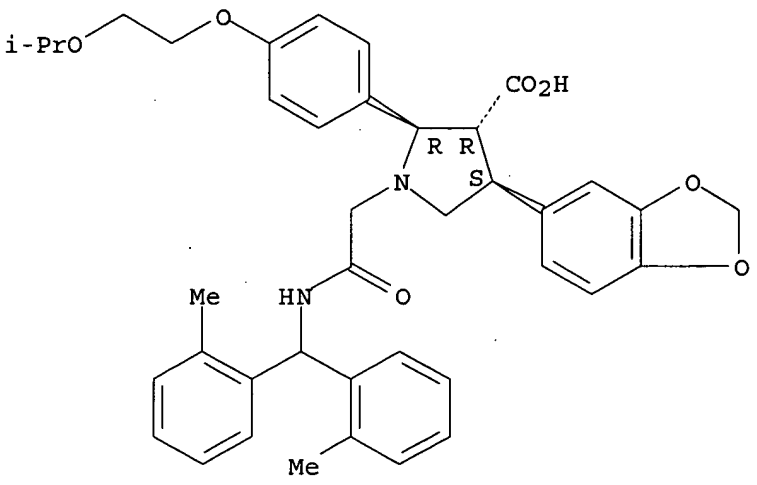
RN 246853-81-6 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-[4-(2-methoxyethoxy)phenyl]-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



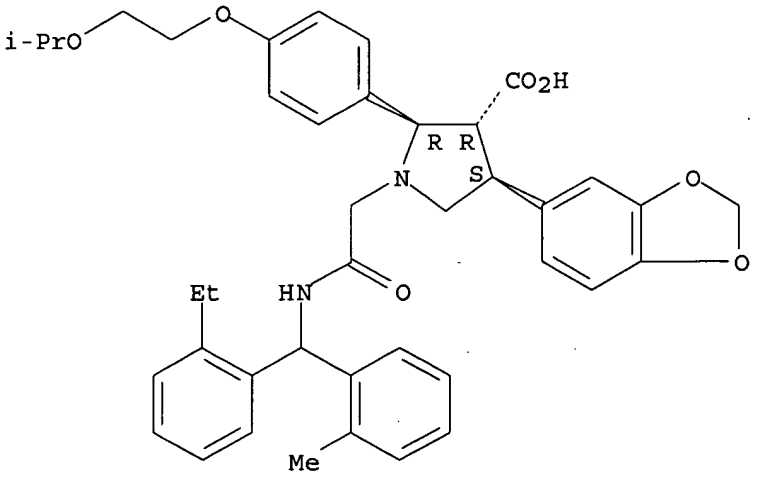
RN 246853-82-7 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-[4-[2-(1-methylethoxy)ethoxy]phenyl]-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



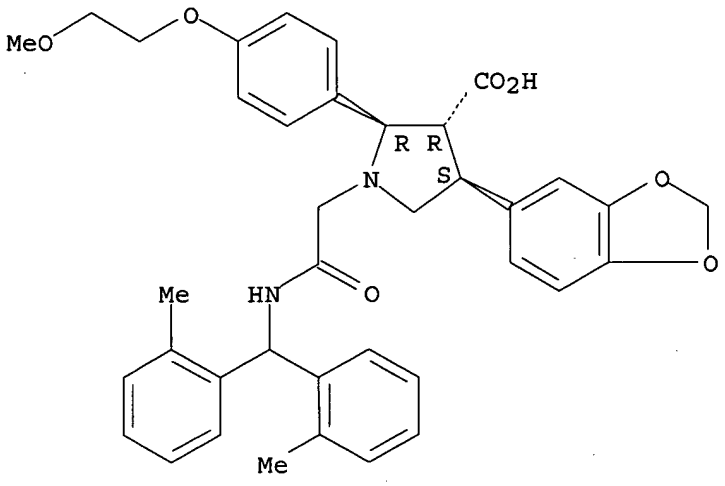
RN 246853-83-8 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[(2-ethylphenyl)(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-[4-[2-(1-methylethoxy)ethoxy]phenyl]-, (2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 246853-85-0 HCAPLUS
CN 3-Pyrrolidinecarboxylic acid, 4-(1,3-benzodioxol-5-yl)-1-[2-[[bis(2-methylphenyl)methyl]amino]-2-oxoethyl]-2-[4-(2-methoxyethoxy)phenyl]-, (2R,3R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



=> d his

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     (FILE 'HOME' ENTERED AT 15:11:53 ON 28 JUN 2005)
               SET COST OFF

     FILE 'REGISTRY' ENTERED AT 15:12:09 ON 28 JUN 2005
L1                STR
L2              0 S L1 CSS
L3                STR L1
L4              1 S L3
L5                STR L3
L6             38 S L5
L7           2808 S L5 FUL
                  SAV L7 SHIAO653/A

     FILE 'HCAPLUS' ENTERED AT 15:17:00 ON 28 JUN 2005
L8              6 S (US94-293349# OR US94-334717# OR US95-442575# OR US95-497998#
L9              1 S US2000-653563#/AP,PRN
                  E WINN M/AU
L10           155 S E3-E9,E13
                  E BOYD S/AU
L11           101 S E3,E4
                  E BOYD STEVE/AU
L12            60 S E4,E5
                  E HUTCHINS C/AU
L13            70 S E3,E10,E13,E16,E17
                  E JAE H/AU
L14            43 S E5,E13,E14
                  E TASKER A/AU
L15            63 S E3,E8,E9
                  E ON GELDERN T/AU
                  E VON GELDERN T/AU
L16            92 S E3-E8
                  E VONGELDERN T/AU
L17             3 S E4
                  E GELDERN T/AU
L18             1 S E4
                  E KESTER J/AU
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L19          25 S E3,E11-E14
                E SORENSEN B/AU
L20          16 S E3,E8
L21          40 S E46
                E SZCZEPANKIEWICZ B/AU
L22          43 S E4-E7
                E HENRY K/AU
                E SZCZEPANKIEWICZ B/AU
L23           1 S E2
                E HENRY K/AU
L24          15 S E3,E7
L25          34 S E35,E37-E39
                E LIU G/AU
L26         843 S E3-E29
                E LIU GANG/AU
L27         869 S LIU GANG?/AU
                E WITTENBERGER S/AU
L28          61 S E4-E8
                E KING S/AU
L29          54 S E3,E4
                E KING STEVE/AU
L30          71 S E3,E4,E7-E9
                E JANUS T/AU
L31          15 S E4,E6,E7
                E PADLEY R/AU
L32          28 S E4-E6
                E ABBOT/PA,CS
L33         147 S E3,E4
                E ABBOTT/PA,CS
L34        8778 S E3,E4
L35         197 S L7
L36           1 S L9 AND L35
L37          54 S L8-L34 AND L35
L38          54 S L36,L37
L39           0 S L38 AND (PY<=1994 AND PRY<=1994 OR AY<=1994)
L40           6 S L35 AND (PY<=1994 AND PRY<=1994 OR AY<=1994)
L41          10 S L35 AND (PY<=1995 AND PRY<=1995 OR AY<=1995)
L42           3 S L38 AND L41
L43           7 S L41 NOT L42
L44           2 S L43 NOT 74/SC,SX
L45           4 S L36,L42

     FILE 'REGISTRY' ENTERED AT 15:34:48 ON 28 JUN 2005

     FILE 'HCAPLUS' ENTERED AT 15:35:13 ON 28 JUN 2005
                SET SMARTSELECT ON
L46          SEL L45 1- RN :    2839 TERMS
                SET SMARTSELECT OFF

     FILE 'REGISTRY' ENTERED AT 15:35:15 ON 28 JUN 2005
L47         2839 S L46
L48         2273 S L7 AND L47

     FILE 'HCAPLUS' ENTERED AT 15:36:19 ON 28 JUN 2005
                SET SMARTSELECT ON
L49          SEL L36 1- RN :     669 TERMS
                SET SMARTSELECT OFF

     FILE 'REGISTRY' ENTERED AT 15:36:20 ON 28 JUN 2005
L50          669 S L49
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L51          287 S L7 AND L50
L52            0 S L1 CSS SAM SUB=L7
L53            7 S L1 CSS FUL SUB=L7
                 SAV L53 SHIAO653A/A

     FILE 'HCAOLD' ENTERED AT 15:38:25 ON 28 JUN 2005
L54            0 S L53

     FILE 'HCAPLUS' ENTERED AT 15:38:30 ON 28 JUN 2005
L55            3 S L53
                 S L55 AND L1-L34

     FILE 'REGISTRY' ENTERED AT 15:38:43 ON 28 JUN 2005

     FILE 'HCAPLUS' ENTERED AT 15:38:44 ON 28 JUN 2005
L56            2 S L55 AND L8-L34
                 E HWAN SOO/AU
L57            1 S E5
                 E HWAN S/AU
L58            2 S L56,L57

     FILE 'USPATFULL, USPAT2' ENTERED AT 15:39:58 ON 28 JUN 2005
L59            0 S L53

     FILE 'REGISTRY' ENTERED AT 15:40:17 ON 28 JUN 2005
L60              STR L1
L61           22 S L60 CSS FUL SUB=L7
                 SAV L61 SHIAO653B/A

     FILE 'HCAOLD' ENTERED AT 15:43:06 ON 28 JUN 2005
L62            0 S L61

     FILE 'HCAPLUS' ENTERED AT 15:43:08 ON 28 JUN 2005
L63            3 S L61
L64            2 S L63 AND L8-L34,L56-L58
L65            1 S L63 NOT L64

     FILE 'USPATFULL, USPAT2' ENTERED AT 15:43:54 ON 28 JUN 2005
L66            0 S L61

     FILE 'REGISTRY' ENTERED AT 15:44:05 ON 28 JUN 2005

     FILE 'HCAPLUS' ENTERED AT 15:44:18 ON 28 JUN 2005

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